What is claimed is:

1. An isolated nucleic acid molecule encoding a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein.

2. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is a DNA molecule.

3. The isolated DNA molecule of claim 2, wherein the DNA molecule is a cDNA molecule.

4. The isolated DNA molecule of claim 2, wherein the DNA molecule is a genomic DNA molecule.

5. The isolated nucleic acid of claim 1, wherein the nucleic acid molecule is an RNA molecule.

6. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule encodes a mammalian Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein.

7. The isolated nucleic acid molecule of claim 1, wherein the mammalian Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein is a mouse, rat, or human Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein.

8. The isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein comprising an

amino acid sequence as set forth in Figure 7B (SEQ ID NO:2).

9. The isolated nucleic acid molecule of claim 8, wherein the amino acid sequence comprises an isoleucine zipper motif and a hereditary multiple extoses C (EXT C) domain.

10. The isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein, wherein the Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein has substantially the same amino acid sequence as set forth in Figures 7B (SEQ ID NO: 2).

11. The isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein, wherein the Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein has the amino acid sequence as set forth in Figure 7B (SEQ ID NO: 2).

12. The isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein comprising an amino acid sequence as set forth in Figure 8B (SEQ ID NO:4).

13. The isolated nucleic acid molecule of claim 12, wherein the amino acid sequence comprises an isoleucine zipper motif and a hereditary multiple

extoses C (EXT C) domain.

14. The isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein, wherein the Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein has substantially the same amino acid sequence as set forth in Figure 8B (SEQ ID NO:4).

15. The isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein, wherein the Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein has the amino acid sequence as set forth in Figure 8B (SEQ ID NO: 4).

16. An isolated nucleic acid molecule encoding a mutant homolog of the mammalian Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein whose genetic alteration is set forth in Table 3.

17. The isolated nucleic acid molecule of claim 12, which is a deletion mutant.

18. The deletion mutant of claim 17, wherein the encoded mutant homolog comprises a tumor suppressor locus.

19. The deletion mutant of claim 17, wherein the encoded mutant homolog does not comprise a tumor suppressor

locus domain.

20. The isolated nucleic acid molecule of claim 6, wherein the mammalian TREX comprises a mouse nucleic acid sequence set forth in Figure 7A (SEQ ID NO:1).

21. The isolated nucleic acid molecule of claim 6, wherein the mammalian TREX comprises a human nucleic acid sequence set forth in Figure 8A (SEQ ID NO:3).

22. A vector comprising the nucleic acid molecule of claim 1.

23. The vector of claim 22 adapted for expression in a host cell which comprises the regulatory elements necessary for expression of the nucleic acid molecule in the host cell operatively linked to the nucleic acid molecule encoding the Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein so as to permit expression of the TREX protein.

24. The vector of claim 23, wherein the host cell is a eukaryotic, bacterial, insect or yeast cell.

25. The vector of claim 24, wherein the eukaryotic host cell is a mammalian cell.

26. The vector of claim 25, wherein the vector is a plasmid.

27. A vector comprising the nucleic acid molecule of claim 3.

28. The vector of claim 27 adapted for expression in a host cell which comprises the regulatory elements

necessary for expression of the nucleic acid molecule in the host cell operatively linked to the nucleic acid molecule encoding the Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein as to permit expression of the TREX protein.

29. The vector of claim 28, wherein the host cell is a eukaryotic, bacterial, insect or yeast cell.

30. The vector of claim 29, wherein the eukaryotic host cell is a mammalian cell.

31. The vector of claim 30, wherein the vector is a plasmid.

32. A method of producing a host cell operatively linked to the nucleic acid molecule encoding a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein, which comprises growing a host cell comprising the vector of claim 29 under suitable conditions permitting production of the TREX protein and recovering the TREX protein so produced.

33. The method of claim 32, further comprising purifying the recovered TREX protein.

34. A method of producing a polypeptide having the biological activity of a protein encoded by the nucleic acid molecule encoding a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein which comprises growing the host cells of claim 29 under suitable conditions permitting production of the polypeptide and recovering the polypeptide so produced.

35. The method of claim 34, further comprising purifying the recovered polypeptide.

36. A purified mammalian Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein.

37. The purified mammalian Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein of claim 36 which is a human TREX protein.

38. A protein comprising substantially the amino acid sequence set forth in Figure 7A.

39. A protein comprising substantially the amino acid sequence set forth in Figure 8A.

40. An oligonucleotide comprising a nucleic acid molecule of at least 15 contiguous nucleotides capable of specifically hybridizing with a unique sequence included within the sequence of the isolated nucleic acid molecule encoding a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein of claim 1.

41. The oligonucleotide of claim 40, wherein the nucleic acid is DNA.

42. The oligonucleotide of claim 40, wherein the nucleic acid is RNA.

43. An antisense oligonucleotide comprising a sequence capable of specifically hybridizing with a unique sequence included within the mRNA molecule of claim 5.

44. An antisense oligonucleotide comprising a sequence capable of specifically hybridizing with a unique sequence included within the genomic DNA molecule of claim 4.

45. An antibody capable of binding to the protein of any of claims 36, 37, 38 and 39.

46. An antibody capable of binding to the protein of any of claims 36, 37, 38 and 39, wherein the antibody is a monoclonal antibody.

47. An antibody capable of binding to the protein of any of claims 36, 37, 38 and 39, wherein the antibody is a polyclonal antibody.

48. A monoclonal antibody directed to an epitope of a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein.

49. A method of inhibiting TREX protein interaction with a TRAF protein comprising administering a ligand comprising an amino acid domain which binds to a EXT C domain of the TREX protein so as to inhibit binding of the TREX protein to the TRAF protein.

50. A method of inhibiting overexpression of TREX protein comprising administering the antisense oligonucleotide of claim 43 which binds to an mRNA molecule encoding a human Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein so as to inhibit overexpression of the human TREX protein.

51. The method of claim 50, wherein inhibiting

overexpression of TREX protein thereby inhibits TRAF-induced CD40 signal dependent NF-kB activation.

52. The method of claim 49, wherein the ligand is an antibody capable of binding to the TREX protein.

53. The method of claim 52, wherein the antibody is a monoclonal or a polyclonal antibody.

54. A method of inhibiting growth of a tumor cell comprising blocking a TRAF interacting site of a TREX protein by administering a ligand capable of binding to the TRAF interacting site of a TREX protein.

55. The method of claim 54, wherein the TRAF interacting site is a hereditary multiple extoses C (EXT C) domain.

56. The method of claim 55, wherein the tumor cell growth is inhibited <u>in vivo</u> or <u>in vitro</u>.

57. The method of claim 56, wherein the ligand is an antibody capable of binding to the TRAF interacting site of a TREX protein.

58. The method of claim 57, wherein the antibody is a monoclonal or a polyclonal antibody.

59. A pharmaceutical composition comprising an amount of the oligonucleotide of any one of claims 40, 41, 42, 43, or 44, effective to prevent overexpression of a TREX protein and a pharmaceutically acceptable carrier capable of passing through a cell membrane.

60. A pharmaceutical composition comprising an amount of the antibody of any one of claims 45, 46 or 47

effective to block binding of a TREX protein to a TRAF protein and a pharmaceutically acceptable carrier capable of passing through a cell membrane.

61. A method of treating an abnormality in a subject, wherein the abnormality is alleviated by the inhibition of binding of a TREX protein and a TRAF protein which comprises administering to the subject an effective amount of the pharmaceutical composition of claim 60 effective to block binding of the TREX protein and the TRAF protein in the subject, thereby treating the abnormality in the subject.

62. The method of claim 61, wherein the TRAF protein is TRAF2, TRAF3 or TRAF 5.

63. The method of claim 62, wherein the abnormality is cancer, a hereditary multiple extosis or an autoimmune disease.

64. The method of claim 63, wherein the cancer is colon cancer, gastric cancer, human head and neck squamous cell carcinoma, prostate carcinoma, breast cancer, thyroid cancer, esophageal cancer, lung cancer, colorectal cancer, ovarian cancer, papillary bladder cancer, osteosarcoma, chondrosarcoma, liposarcoma, giant cell tumor, Ewing sarcoma, or other malignant tumors.

65. A method of treating an abnormality in a subject, wherein the abnormality is alleviated by the inhibition of overexpression of a TREX protein which comprises administering to the subject an effective amount of the pharmaceutical composition of claim 53 effective to inhibit overexpression of the TREX protein, thereby treating the abnormality in the

subject.

66. The method of claim 65, wherein the abnormality is cancer, a hereditary multiple extosis or an autoimmune disease.

67. The method of claim 66, wherein the cancer is colon cancer, gastric cancer, human head and neck squamous cell carcinoma, prostate carcinoma, breast cancer, thyroid cancer, esophageal cancer, lung cancer, colorectal cancer, ovarian cancer, papillary bladder cancer, osteosarcoma, chondrosarcoma, liposarcoma, giant cell tumor, Ewing sarcoma, or other malignant tumors.

68. A method of screening for a chemical compound which inhibits TREX protein and TRAF protein binding comprising:

(a) incubating the chemical compound with a TREX protein and a TRAF protein;

(b) contacting the incubate of step (a) with an affinity medium under conditions so as to bind a TREX protein-TRAF protein complex, if such a complex forms; and

(c) measuring the amount of the TREX protein-TRAF protein complex formed in step (b) so as to determine whether the compound is capable of interfering with the formation of the complex between the TREX protein-TRAF protein.

69. The method of claim 68, wherein the TRAF is a TRAF2, TRAF3 or a TRAF 5.

70. The method of claim 69, wherein the compound is a CD40 receptor ligand.

71. The method of claim 69, wherein the molecule is a

peptide or a fragment thereof which comprises a TRAF binding domain.

72. The method of claim 71, wherein the TRAF is a TRAF2, TRAF3 or a TRAF 5.

73. A method of preventing inhibition of a CD40 signal-dependent NF-kB activation comprising administering the antisense oligonucleotide of claim 37 which binds to an mRNA molecule encoding a human Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein so as to prevent inhibition of activation of CD40 signal-dependent NF-kB activation.

74. A method of preventing inhibition of a CD40 signal-dependent NF-kB activation comprising administering a ligand comprising an amino acid domain which binds to a EXT C domain of the TREX protein so as to inhibit binding of the TREX protein to the TRAF protein, thereby preventing inhibition of a CD40 signal-dependent NF-kB activation.

75. The method of claim 74, wherein the ligand is peptide or a fragment thereof which comprises a TRAF binding domain.

76. A method of preventing upregulation of a TNF receptor typeII signal-dependent NF-kB activation comprising administering the antisense oligonucleotide of claim 37 which binds to an mRNA molecule encoding a human Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein so as prevent upregulation of a TNF receptor typeII signal-dependent NF-kB activation.

77. A method of preventing upregulation of activation of a TNF receptor typeII-signal-dependent NF-kB comprising administering a ligand comprising an amino acid domain which binds to a EXT C domain of the TREX protein so as to inhibit binding of the TREX protein to the TRAF protein, thereby preventing upregulation of activation of a TNF receptor typeII-signal-dependent NF-kB.

78. The method of claim 77, wherein the ligand is peptide or a fragment thereof which comprises a TRAF binding domain.

79. A method of detecting a predisposition to cancer which comprises detecting of a mutation in a nucleic acid encoding TREX protein in the sample from the subject.

80. The method of claim 79, wherein the mutation is a silent point mutation or a missense point mutation.

81. The method of claim 79, wherein the mutation in the nucleic acid encoding TREX protein is detected by contacting the nucleic acid from the sample with a TREX nucleic acid probe under conditions permitting the TREX nucleic acid probe to hybridize with the nucleic acid from the sample, thereby detecting the mutation in the nucleic acid encoding TREX protein in the sample.

82. The method of claim 81, wherein the cancer is colon cancer, gastric cancer, human head and neck squamous cell carcinoma, prostate carcinoma, breast cancer, thyroid cancer, esophageal cancer, lung cancer, colorectal cancer, ovarian cancer, papillary bladder cancer, osteosarcoma, chondrosarcoma, liposarcoma, giant cell tumor, Ewing sarcoma, or other malignant

tumors.

83. The method of claim 81, wherein the TREX nucleic acid probe comprises a nucleic acid molecule of at least 15 nucleotides which specifically hybridizes with a unique sequence included within the sequence of an isolated nucleic acid molecule encoding a Tumor necrosis factor Receptor-Associated Factor (TRAF) protein-interacting hereditary multiple extoses (TREX) protein.

84. The TREX nucleic acid probe of claim 81, wherein the nucleic acid is DNA.

85. The TREX nucleic acid probe of claim 81, wherein the nucleic acid is RNA.

86. A TREX nucleic acid probe comprising a sequence capable of specifically hybridizing with a unique sequence included within the DNA molecule of claim 2.

87. A TREX nucleic acid probe comprising a sequence capable of specifically hybridizing with a unique sequence included within the mRNA molecule of claim 5.

88. The TREX nucleic acid probe comprising a sequence capable of specifically hybridizing with a unique sequence included within the genomic DNA molecule of claim 4.

89. The method of claim 79, wherein the mutation comprises a portion of a tumor suppressor locus.

90. The method of diagnosing cancer in a subject which comprises:

a) obtaining DNA from the sample of a subject suffering from cancer;

b) performing a restriction digest of the DNA with a panel of restriction enzymes;

c) separating the resulting DNA fragments by size fractionation;

d) contacting the resulting DNA fragments with a nucleic acid probe capable of specifically hybridizing with a unique sequence included within the sequence of a genetic alteration of a nucleic acid molecule encoding a TREX protein, wherein the nucleic acid is labeled with a detectable marker;

e) detecting labeled bands which have hybridized to the nucleic acid probe in step (d), wherein the sequence of a genetic alteration of a nucleic acid molecule encoding a TREX protein creates a unique band pattern specific to the DNA of subjects suffering from cancer;

f) preparing DNA obtained from a sample of a subject for diagnosis by steps (a-e); and

g) comparing the detected band pattern specific to the DNA obtained from a sample of subjects suffering from cancer from step (e) and the DNA obtained from a sample of the subject for diagnosis from step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to cancer if the patterns are the same.

91. The method of claim 90, wherein the size fractionation in step (c) is effected by a

polyacrylamide or agarose gel.

92. The method of claim 90, wherein the detectable marker is radioactive isotope, enzyme, dye, biotin, a fluorescent label or a chemiluminescent label.

93. A method of diagnosing cancer in a subject which comprises:

a) obtaining RNA from the sample of the subject suffering from cancer;

b) separating the RNA sample by size fractionation;

c) contacting the resulting RNA species with a nucleic acid probe capable of specifically hybridizing with a unique sequence included within the sequence of a nucleic acid molecule encoding a mutated TREX protein, wherein the sequence of the nucleic acid molecule encoding the mutated TREX protein is labeled with a detectable marker;

d) detecting labeled bands which have hybridized to the RNA species to create a unique band pattern specific to the RNA of subjects suffering from cancer;

e) preparing RNA obtained from a sample of a subject for diagnosis by steps (a-d); and

f) comparing the detected band pattern specific to the RNA obtained from a sample of subjects suffering from cancer from step (d) and the RNA obtained from a sample of the subject for diagnosis from step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to cancer if the patterns are the same.

94. The method of claim 93, wherein the size fractionation in step (c) is effected by a polyacrylamide or agarose gel.

95. The method of claim 93, wherein the detectable marker is radioactive isotope, enzyme, dye, biotin, a fluorescent label or a chemiluminescent label.

96. The method of either of claim 90 or 93, wherein cancer associated with the expression of a mutated TREX protein is diagnosed.

97. The method of either of claim 90 or 93, wherein the cancer is colon cancer, gastric cancer, human head and neck squamous cell carcinoma, prostate carcinoma, breast cancer, thyroid cancer, esophageal cancer, lung cancer, colorectal cancer, ovarian cancer, papillary bladder cancer, osteosarcoma, chondrosarcoma, liposarcoma, giant cell tumor, Ewing sarcoma, or other malignant tumors.

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